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# Reliability of detecting fundus abnormalities associated with systemic hypertension in cats assessed by veterinarians with and without ophthalmology specialty training

**Inaugural Thesis**

to obtain the title of Doctor from the
Vetsuisse Faculty University of Zurich

submitted by

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Reliability of detecting fundus abnormalities associated with systemic hypertension in cats assessed by veterinarians with and without ophthalmology specialty training

Systemic hypertension (SHT) causes target organ damage (TOD) and measuring blood pressure (BP) should be routine in risk populations. Fundoscopy corroborates relevance of high BP results and decides on immediate therapy. Not every cat can be seen by an ophthalmologist. The objective was to determine reliability of fundoscopy in cats with SHT performed by a veterinarian without ophthalmology specialty training. Cats with suspicion of hypertensive TOD or belonging to a risk population for SHT with BP >160 mmHg were enrolled. Indirect ophthalmoscopy was performed by a recent graduate veterinarian followed by a veterinary ophthalmologist. Thirty-tree cats were included. In 27 SHT was confirmed. In 12 of 27 SHT was detected on routine examinations; fundus lesions were seen in 9 by the non-trained veterinarian, in 11 by an ophthalmologist. Nine of the 27 were neurological patients; fundus lesions were seen in 4 by the non-trained, in 7 by an ophthalmologist. Six of the 27 were presented for blindness; fundus lesions were seen in all by the non-trained veterinarian and an ophthalmologist. In 6 of 33 cats, SHT was not confirmed. Compared to an ophthalmologist, reliability of detecting ocular TOD by the non-trained veterinarian was 72% for cats with and 100% for cats without vision. Fundoscopy by a non-speciality trained veterinarian has a reasonably high reliability to detect ocular TOD. Private practice veterinarians are encouraged to perform a fundic exam in cats with SHT.

Keywords: blood pressure, feline hypertensive oculopathy, situational hypertension, Doppler sphygmomanometry, target organ damage

## Summary German

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Reliability of detecting fundus abnormalities associated with systemic hypertension in cats assessed by veterinarians with and without ophthalmology specialty training

Systemische Hypertension (SHT) verursacht Endorganschaden (EOS) und Blutdruck (BD) sollte in Risikopopulationen routinemässig gemessen werden. Die Fundoskopie bestätigt die Relevanz von hohen BD-Messungen und entscheidet über sofortigen Therapiebeginn. Nicht alle Katzen können vom Spezialisten gesehen werden. Das Ziel war es, die Sensitivität der Fundoskopie bei Katzen mit SHT durch einen ophthalmologisch unerfahrenen Veterinär (LM) zu bestimmen. Katzen mit Verdacht für hypertensiven EOS oder aus Risikopopulationen mit einem BD >160 mmHg wurden inkludiert. Indirekte Ophthalmoskopie wurde zuerst durch LM, danach durch einen Opthtalmologen durchgeführt. Dreiunddreissig Katzen wurden eingeschlossen. In 27 wurde SHT bestätigt. In 12 von 27 wurde SHT bei Routineuntersuchung diagnostiziert; Fundusläsionen wurden in 9 durch LM und in 11 durch den Ophthalmologen gefunden. Neun von 27 waren neurologische Patienten; Fundusläsionen wurden in 4 durch LM und in 7 durch den Ophthalmologen gefunden. Sechs von 27 wurden blind präsentiert; Fundusläsionen wurden durch beide Untersucher in allen gefunden. In 6 von 33 Katzen wurde SHT nicht bestätigt. Im Vergleich zum Ophthalmologen, betrug die Sensitivität der Fundoskopie durch LM 72% bei Katzen mit und 100% ohne Sehvermögen. Die Fundoskopie durch einen ophthalmologisch unerfahrenen Veterinär hat eine relevante Sensitivität um okulären EOS zu detektieren. Privattierärzte werden ermutigt, Fundusuntersuchungen in Katzen mit SHT durchzuführen.

Stichworte: Blutdruck, feline hypertensive Retinopathie, situative Hypertension, Doppler-Sphygmomanometrie, Endorganschaden

## Introduction

Systemic hypertension (SHT) is a well-recognized problem in elderly cats. Chronic kidney disease (CKD), hyperthyroidism, a combination of both diseases and hyperaldosteronism represent common underlying diseases. In addition, idiopathic SHT accounts for up to 40% of cases.[1,2,3,4,5] Persistent elevated blood pressure (BP) can lead to target organ damage (TOD), particularly in the eye, followed by the central nervous system (CNS), kidneys and the cardiovascular system.[6,7,8,9,10,11] Hypertensive cats often present in an advanced stage of TOD with a guarded prognosis quo ad restitutionem.[1,6] The fundus abnormalities in SHT are thought to occur in the following sequence of events: SHT causes autoregulatory vasoconstriction of retinal arterioles visible as focal narrowing (beading) of these vessels, and causing remodeling of the smooth muscle layer, ischemic damage and degeneration of the endothelium when persistent. Ultimately, focal disintegration and rupture of the vessel walls can lead to leakage of plasma and blood, causing vessel-associated focal retinal edema and intraretinal hemorrhages. More widespread retinal edema, bullous intraretinal fluid accumulation and larger intraretinal and preretinal hemorrhages can occur in later stages of the disease. Retinal detachment is most likely a direct result of plasma effusion from the choroidal vasculature with ischemic damage to the retinal pigment epithelium as contributing factor. Optic nerve ischemia leads to papilledema and in the end-stage to optic atrophy. Clinically, the ocular manifestations include retinal arterial tortuosity and beading, retinal edema, pre-, intra- and subretinal hemorrhages, focal bullous intraretinal fluid accumulation, retinal detachment, retinal degeneration, papilledema and optic atrophy. Pathologies associated with plasma effusion into the choroid and optic nerve can occur in parallel to retinal vessel associated changes.[1,12,13] Additional potential ocular complications of systemic hypertension include anterior segment and vitreous hemorrhage, uveitis, and glaucoma.[2,6,7]
Routine screening for SHT in at-risk populations is good clinical practice and an important preventive task.[11] However, non-invasive BP measurement in cats is not always reliable and particularly situational hypertension is an important reason for elevated BP measurements implying SHT.[3,4,14] Whereas antihypertensive treatment should not be delayed in true hypertensive cats to prevent potentially irreversible SHT, overtreating cats without real SHT is not advised. Therefore, in cats without TOD repeated BP measurements at different time points are necessary for a definitive diagnosis of SHT and to justify lifelong antihypertensive treatment.[11] Retinal examination in an asymptomatic cat with a high BP measurement is an important step to detect TOD and to decide on immediate antihypertensive treatment. If lesions compatible with TOD are found, the diagnosis of SHT can be considered established and antihypertensive treatment should not be delayed.[11] Detecting early stages of ocular TOD affects the prognosis of regaining vision.[15] However, in general practice most cats with a high BP measurement cannot be examined immediately by an ophthalmologist.
Thus, the aim of this study was to evaluate the reliability of fundoscopic examination for identifying TOD in cats with SHT performed by a new graduate veterinarian without ophthalmology specialty training (LM) compared to a veterinarian with specialty training in ophthalmology.

## Materials and Methods

### *Animals*

The study population consisted of client-owned cats presented to any service of the Small Animal Clinic, Vetsuisse Faculty University of Zurich, between March 2019 and August 2020 with a clinical complaint potentially associated with SHT or predisposing for SHT, in whom an elevated BP had been measured. Specifically, these were cats characterized by one criterion of the following a) acute onset of blindness, b) central nervous system signs localized to the cerebrum (e.g. seizures) in an elderly cat, c) predisposing underlying diseases such as CKD and/or hyperthyroidism, d) age >10 years at a routine examination. A routine complete blood count and biochemical profile were performed to identify underlying diseases. Abdominal ultrasound was performed in cats with serum potassium <3.8 mmol/l to particularly assess the adrenal glands as an indicator of potential hyperaldosteronism.
Cats were classified as having CKD if the concentration of serum creatinine was above the reference range (98-163 umol/l), in non-dehydrated animals with or without clinical signs such as weight loss, polyuria/ polydipsia or abnormal kidneys on palpation (irregular size and / or surface). Cats were classified as being hyperthyroid if the concentration of serum T4 exceeded the reference range (>3.3 mcg/dl). Conn syndrome was diagnosed if an adrenal mass was found on abdominal ultrasound and serum aldosterone was elevated in a hypokalemic cat. SHT was classified as primary or idiopathic if no apparent underlying cause was identified.

### *BP measurement*

Indirect BP measurements were obtained by Doppler sphygmomanometry (Parks Device 811B) using a standard protocol. In brief, the limb circumference was measured in order to choose the appropriate cuff size (table 1). As soon as repeated BP measurements plateaued, the average of the 5 subsequent consecutive measurements was obtained. Cats were included, if this average systolic BP was >160 mmHg. The first BP measurements were obtained by the attending clinician or LM; all subsequent BP measurements were performed by LM. Cats were defined as truly hypertensive if fundus lesions consistent with SHT were observed, and as not hypertensive if no fundus lesions were observed and repeated BP measurements were <160 mmHg.

### *Fundoscopy*

Pharmacological mydriasis was induced via topical application of tropicamide 0.5% eyedrops (Thea Pharma SA) 20 minutes prior to the examination to optimize visibility of the ocular fundus. Pharmacological pupil dilation was omitted if cats presented with persistent mydriasis. Monocular indirect ophthalmoscopy was first performed in each cat by the new graduate veterinarian without ophthalmology specialty training (LM) using a 28D indirect condensing lens (Volk) and a Finoff transilluminator (Heine). The cat was held in a sternal position in a darkened room with the help of an assistant to keep the cats’ eyelids open. The light source was positioned against the temple of the examiner and was directed towards the patient’s eye. Once the tapetal

reflex was identified, the indirect condensing lens was placed in front of the eye of the cat to allow examination of the ocular fundus. The use of a 28D indirect condensing lens and Finoff transilluminator to perform fundoscopy was chosen as these devices are readily available and affordable to the general practitioner. Furthermore, 28D lenses allow relatively easy positioning and manipulation of the lens in combination with a wide-angle view of the fundus.
Subsequently, fundic examination was performed through binocular indirect ophthalmoscopy by a trained ophthalmologist using 28, 20 and/or 15D condensing lenses (Volk) and a Heine Omega 500 binocular indirect ophthalmoscope (Heine). The use of a binocular ophthalmoscope is advantageous for the evaluation of fundus lesions since it allows stereopsis and thus increases depth perception. The use of 20 and 15D lenses, which have less condensing power than a 28D lens, increases magnification of fundus details and increases depth perception while simultaneously shrinking the field of view of the fundus. Pictures of the fundus were taken using a fundus camera (Smartscope pro, Optomed).

## Results

### *Animals, blood pressure, underlying diseases*

Selected results for all cats are presented in table 2, with the cats listed according to the sequence of their enrolment into the study.
Thirty-three cats were enrolled with a BP >160 mmHg at first measurement. Of these 33 cats, 27 were diagnosed as being truly hypertensive because of the presence of TOD or based on subsequent BP measurements. Six of the 27 cats were presented because of acute onset of blindness. Nine of the 27 cats were presented because of neurological signs (seizures, ataxia, torticollis, nystagmus or intermittent strange behaviour); of these, five had been referred for a neurological work-up. Twelve of the 27 cats were not presented because of clinical signs suggesting TOD, but had SHT identified on routine BP measurement. Breeds included Domestic Shorthair and Domestic Longhair (21), Siamese (2), British Shorthair (1), Burmese (1), Persian (1) and Norwegian Forest Cat (1). Thirteen of the cats were spayed females and fourteen cats were neutered males. An abdominal ultrasound to rule out hyperaldosteronism was performed in six cats with low serum potassium, all with negative results.
In 6 of the 33 enrolled cats, SHT was not confirmed on subsequent BP measurements; these six cats comprised the negative controls. Breeds included Domestic Shorthair (5) and British Shorthair (1). Three of the cats were spayed females and three were neutered males.
The median systolic BP in the six cats with blindness as primary concern was 208 mmHg (190-270 mmHg). Their median age was 17 years (13-19 years). The underlying diseases were CKD (n=2), concurrent CKD and hyperthyroidism (n=1) and idiopathic SHT (n=3).
The median systolic BP in the nine cats with neurological signs as primary concern was 230 mmHg (161-283 mmHg). Their median age was 16 years (10-17 years). The underlying diseases were CKD (n=4), hyperthyroidism (n=2) and idiopathic SHT (n=3).
The median systolic BP in the twelve cats with SHT as primary concern was 206 mmHg (166-263 mmHg). Their median age was 15 years (range 2-17 years). The

underlying diseases were CKD (n=6), hyperthyroidism (n=3), concurrent CKD and hyperthyroidism (n=1) and idiopathic SHT (n=2).
The median systolic BP in the six control cats was 188 mmHg (180-220 mmHg). Their median age was 14 years (11-16.5 years). The primary reasons for BP measurement in these cats were hyperthyroidism (n=2) or age >10 years (n=4).

### *Fundoscopy*

Fundus lesions were detected both by LM and by the attendant ophthalmologist in all six cats presented with blindness due to STH. The attendant ophthalmologist identified ocular TOD in seven of nine cats with neurological signs, whereas LM correctly identified TOD in four of these seven cats. The attendant ophthalmologist identified ocular TOD in eleven of twelve cats with primary concern SHT, whereas LM correctly identified TOD in nine of these eleven cats. In summary, 24 of 27 cats with STH had ocular TOD confirmed by the attendant ophthalmologist, with LM correctly identifying TOD in 19 of these 24 cats. LM identified ocular TOD in all cats presenting with blindness (sensitivity 100%) and in 13 of 18 cats with neurological signs or SHT as primary complaint (sensitivity 72%).
Ocular lesions were not detected by either the attendant ophthalmologist or by LM in three cats with confirmed SHT, nor in the six cats with an initial BP >160 mmHg, but no confirmation of SHT on subsequent BP measurements. Thus, LM correctly classified all nine cats without ocular TOD.
Fundic lesions detected by the non-trained ophthalmologist included hemorrhages and retinal detachments, and were usually more severe in nature than the ones that were missed (fig. 1, 2 and 3). Fundic lesions that escaped detection by LM were typically more subtle, including retinal edema, punctate hemorrhages, areas of mild hypo- or hyperreflectivity and tortuous blood vessels, particularly when located peripherally (fig. 4).
A training effect seemed present for the non-trained ophthalmologist during the course of the study: LM missed lesions in four of the first seven cases with fundus abnormalities, whereas lesions were missed in only one of the subsequent 17 cases with fundus abnormalities (table 2).

## Discussion

The results of this study with focus on fundic examination in cats with suspected SHT allows the conclusion that a non-specialty trained veterinarian can reach a reasonably high sensitivity of detecting hypertensive ocular TOD, whilst not overdiagnosing fundic lesions. Particularly the more obvious fundic lesions can be detected by a non-specialized veterinarian. The sensitivity for detecting hypertensive ocular TOD was 100% in hypertensive cats with acute blindness as presenting complaint both for the veterinarians with and without ophthalmology specialty training. In the hypertensive cats where the presenting complaint was not blindness, i.e. the more challenging cases, the sensitivity for detecting hypertensive ocular TOD was 72%. Thus, non-specialized veterinarians cannot completely replace veterinary ophthalmologists in such cases. However, the argument could be made that delaying antihypertensive treatment may be justifiable if only subtle lesions are present. With good clinical practice, BP measurement will be repeated within days and antihypertensive treatment started if SHT is confirmed. The likelihood of delaying

treatment to the detriment of the patient would probably be small in such cases. As a matter of fact, repeating BP measurements within days is also the lege artis approach if the ophthalmologist does not detect TOD in a cat suspected of SHT.
Of 27 cats with SHT, 15 were presented because of SHT-induced TOD, either neurological or ocular. In an additional 11 of 12 cats in which SHT was detected by BP screening, ocular TOD was detected. Thus, 26 of 27 cats with SHT had some sort of TOD at the time of first presentation to our hospital, and of these, 24 had some degree of ocular TOD. This is comparable to other studies in which the frequency of ocular lesions was as high as 100%.[1,2,9,16] This finding supports the concern that BP evaluation in cats is mostly performed too late. It also supports the recommendation to routinely measure BP in the feline population at risk for SHT, including asymptomatic elderly cats.[17]
The occurrence of neurological signs as presenting complaint in hypertensive cats in this study was comparable to other studies where the prevalence of hypertensive encephalopathy was 29% to 46%.[1,6] Neurological deficits by itself should trigger veterinarians to measure BP in elderly cats, certainly before performing MRT of the brain. Neurological signs are most likely the result of hypertensive encephalopathy in cases where SHT is diagnosed and neurological signs resolve under antihypertensive treatment.

### *Study limitations*

A non-trained veterinarian may not remain non-trained after performing fundus examinations on a number of cats because of the expected training effect. The training effect observed in this study was likely exacerbated since fundic examinations were the focus of this study, i.e. the non-trained veterinarian invested a significant amount of time in autodidactic training by consulting the relevant literature. Nevertheless, the primary obstacle for detecting fundic lesions is the will to actually perform a thorough enough fundic examination that allows a representative view of the retina. This can be attained without a specialized education. Of note is the fact that LM did not receive any ophthalmic examination training that was not part of her veterinary school curriculum prior to conducting this study.
The fact that the detection of fundic lesions in a suspected hypertensive cat is not conclusive proof of a hypertension-induced lesion is a further limitation of this study. Retinal hemorrhages for example, can be induced by several other causes, including coagulopathies, trauma, chorioretinitis or neoplasia.[18,19]
Finally, fundic examination by a veterinary ophthalmologist was defined as the gold standard for the detection of ocular TOD in this study. However, veterinary ophthalmologists performing indirect ophthalmoscopy may also miss lesions on occasion. Advanced imaging modalities, including fundus angiography, scanning laser ophthalmoscopy (cSLO) and optical coherence tomography (OCT) might have detected lesions in cats graded as non-affected in this study.[20] However, the use of such imaging modalities exceeded the possibilities of this study.

## Conclusions

Measuring BP should be part of a routine health check examination in elderly cats. A fundic examination should be performed immediately if an elevated BP at a level that puts a patient at high risk for developing TOD is measured.[10,11] Antihypertensive treatment could then be initiated immediately if evidence of ocular TOD, corroborating the suspected SHT, is detected. The results of this study should encourage general practitioners to perform an initial fundic examination in suspected hypertensive cats.

## Conflict of Interest

The authors do not declare any conflict of interest.

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## Annexes

Table 1: Choice of cuff size for measuring blood pressure in cats.

| Leg circumference [cm] | Cuff width [cm] | Width corresponding % circumference |
|---|---|---|
| 2.5-4.4 | 1 | 40-23 |
| 4.5-6.9 | 2 | 44-29 |
| 7.0-9.9 | 3 | 43-33 |

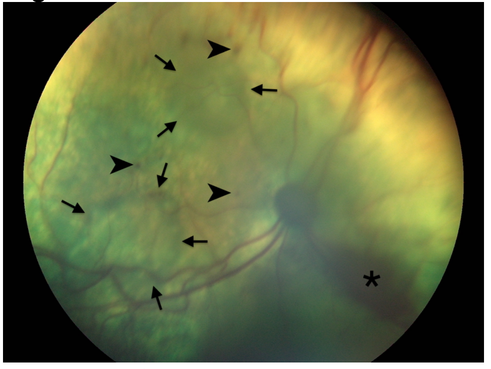
Table 2: Selective results of 33 consecutive feline patients examined for potential hypertensive ocular target organ damage (SHT TOD)

| Case | Age * [years] | BP [mmHg] | Reason for BP measurement | Cause systemic hypertension | Fundoscopy ophthalmologist | Fundoscopy new graduate§ |
|---|---|---|---|---|---|---|
| 1 | 11 | 180 | heart murmur | situational | normal | 1 |
| 2 | 16 | 220 | neuro | situational | normal | 1 |
| 3 | 17.5 | 190 | blind | CKD | brd | 1 |
| 4 | 14 | 190 | T4 | situational | normal | 1 |
| 5 | 14 | 180 | neuro | situational | normal | 1 |
| 6 | 14.5 | 220 | blind | CKD | brd, ph, nph | 1 |
| 7 | 17.5 | 260 | neuro | CKD | brd, ph, nph | 1 |
| 8 | 10.5 | 190 | neuro | CKD | re, tv | 0 |
| 9 | 16.5 | 218 | CKD | situational | normal | 1 |
| 10 | 14.5 | 180 | CKD | CKD + T4 | ph, re | 0 |
| 11 | 17.5 | 161 | neuro | idiopathic | re | 0 |
| 12 | 15 | 200 | neuro | idiopathic | frd | 0 |
| 13 | 10.5 | 263 | CKD | CKD | brd, ph | 1 |
| 14 | 13 | 185 | T4 CM | situational | normal | 1 |
| 15 | 16.5 | 210 | age | idiopathic | frd, ph, re, hyper | 1 |
| 16 | 18 | 270 | blind | idiopathic | brd, ph, nph, hyper | 1 |
| 17 | 15.5 | 230 | CKD | CKD | normal | 1 |
| 18 | 16.5 | 283 | neuro | idiopathic | brd, ph, re, hyper | 1 |
| 19 | 16 | 260 | neuro | T4 | brd | 1 |
| 20 | 11.5 | 243 | age | idiopathic | hyper | 1 |
| 21 | 16.5 | 250 | neuro | CKD | brd, ph, nph | 1 |
| 22 | 15.5 | 227 | neuro | T4 | normal | 1 |
| 23 | 19 | 195 | blind | CKD + T4 | nph, re, hyper | 1 |
| 24 | 17 | 231 | CKD | CKD | re, hypo | 1 |
| 25 | 13.5 | 190 | blind | idiopathic | brd, ph | 1 |
| 26 | 17 | 208 | T4 | T4 | brd, ph, re | 1 |
| 27 | 16 | 226 | blind | idiopathic | brd, nph, hyphema | 1 |
| 28 | 14.5 | 228 | CKD | CKD | normal | 1 |
| 29 | 14 | 189 | CKD | CKD | brd | 1 |
| 30 | 2 | 166 | CKD | CKD | re | 0 |
| 31 | 15 | 187 | T4 | T4 | brd, hyper, hypo | 1 |
| 32 | 15 | 176 | T4 | T4 | brd, re | 1 |
| 33 | 16.5 | 204 | CKD | CKD | re, tv | 1 |

*rounded to the next half year; BP, systolic blood pressure by Doppler sphymomanometry; neuro, clinical abnormalities localized to cerebrum; T4, hyperthyroidism; CKD, chronic kidney disease; T4 CM, hyperthyroidism associated myocardial disease; brd, large bullous retinal detachment; frd, small focal retinal detachment; ph, punctate hemorrhage; nph, non-punctate hemorrhage; re, retinal edema; hyper/hypo, hyper-/hyporeflective areas; tv, tortuous blood vessels. § 1, agreement between veterinarians with and without ophthalmology specialty training in judging fundus to show SHT TOD; 0, disagreement between veterinarians with and without ophthalmology specialty training in judging fundus to show SHT TOD.

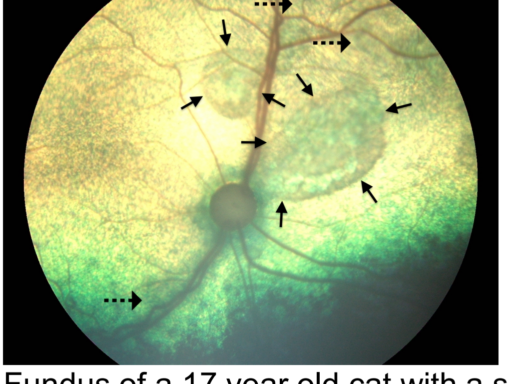
## Figure captions

Figure 1



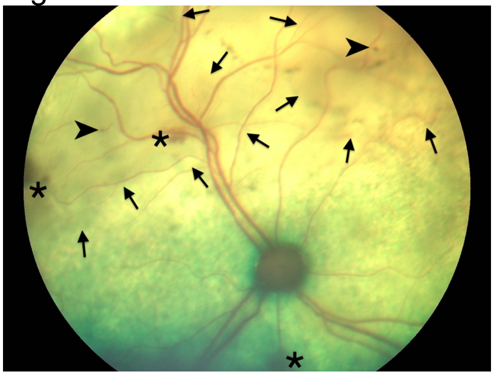

Fundus of a 17.5 year old cat with a systolic blood pressure of 260 mmHg. The presenting complaint was acute vestibular syndrome.
Pathological findings include a nasoventral preretinal hemorrhage of approximately twice the optic nerve head diameter (*), punctate retinal hemorrhages in the temporal and dorsal midperipheral tapetum (arrowheads), and multifocal bullous retinal detachments (arrows).
The generalized haziness of the nasal half of the fundus suggests the presence of either generalized retinal edema or a large flat or mildly elevated retinal detachment.

Figure 2



Fundus of a 17 year old cat with a systolic blood pressure of 208 mmHg. The presenting complaint was diarrhea.
Pathological findings include multifocal bullous retinal detachments (arrows) and areas of focal retinal edema (dashed arrows).

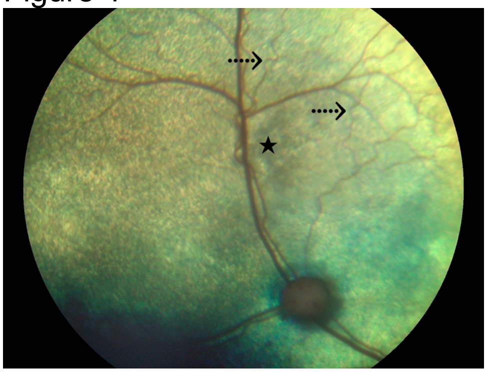
Figure 3



Fundus of a 14.5 year old cat with a systolic blood pressure of 220 mmHg. The presenting complaint was impaired vision.

Pathological findings visible on this image include large dorsal retinal detachments (arrows), punctate hemorrhages (arrowheads) and larger retinal or preretinal hemorrhages (*) and generalized retinal edema as indicated by the fact that the picture seems well focused but a generalized haziness/ loss of fine retinal detail is present in this image. Compare to the crisp detail visible in figure 2.

Figure 4



Fundus of a 10.5 year old cat with a systolic blood pressure of 190 mmHg. The presenting complaint was ataxia.

Pathological findings include an area of tapetal hyporeflectivity (star), a mild tortuosity of blood vessels (dotted arrows) and mild diffuse retinal edema of the nasal retina as indicated by the fact that the picture seems well focused but a generalized haziness/ loss of fine retinal detail is present in the nasal half of the fundus (right-hand side of the image). Compare to the crisp detail visible in figure 2 and in the temporal half of the fundus (left-hand side of the image).

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## Curriculum Vitae

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